

REMARKS

The Examiner's Office Action of June 1, 2005 has been received and its contents reviewed. Claims 1-6 remain pending for consideration, of which claims 1 and 4 are independent. No claims have been amended. In view of the remarks below, Applicants respectfully request reconsideration of this application.

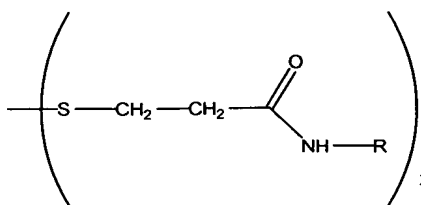
Claim Rejections under 35 U.S.C. § 103(a)

Claims 1-6 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Lewis et al. (U.S. Pat. 3,849,430), Bayer et al. (U.S. Pat. 5,420,290), Hahn et al. (U.S. Pat. 5,453,507), Yen et al. (U.S. Pat. 5,290,512), Lewis et al. (U.S. Pat. 3,523,121) and Jordan (DE 3702546), each taken alone and in combination with each other when similar utilities are asserted. The Examiner's remarks supporting this rejection are found on pages 3-8 of the Office Action. Applicants respectfully traverse this rejection.

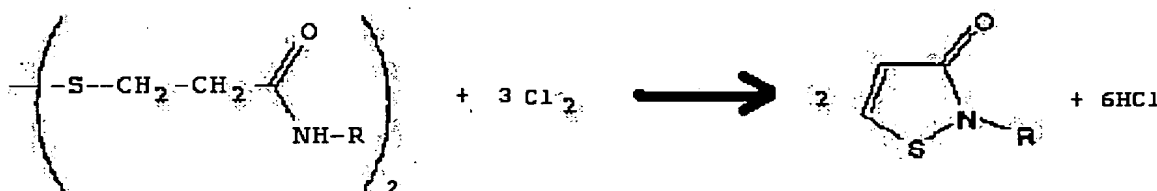
The Examiner asserts that each of the above references teach 2-alkyl-4-isothiazoline-3-one products that are structurally similar to the claimed invention. Furthermore, the Examiner asserts that one skilled in the art would be motivated to prepare products embraced by the prior art but improve on the purity of the active ingredient, 2-alkyl-4-isothiazoline-3-one, to arrive at the instant claimed products with the expectation of obtaining additional beneficial products which would be useful as disinfectant.

The cited references fail to establish a prima facie showing of obviousness because they do not teach or suggest the claimed invention, alone or in combination with each other. Applicants' invention, as claimed in independent claims 1 and 4, relates to an industrial disinfectant composition comprising, as an effective component, a 2-alkyl-4-isothiazoline-3-one, in which the amount of the contaminant, a 5-chloro-2-alkyl-4-isothiazoline-3-one is less than 0.1%, with chlorine as a chlorinating agent in dichloromethane as a solvent, in which hydrogen chloride is insoluble or exhibits low solubility, at a temperature of 39-41°C, with a ratio of three mole equivalents of chlorinating agent per mol of formula (II) in reaction 1.

Formula (II)



Reaction 1



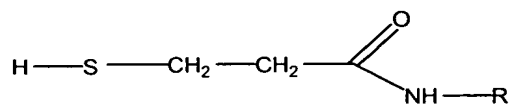
Although the use of 2-alkyl-4-isothiazoline 3-one is known in the art as industrial disinfectants, the composition of the product has always been a mixture of 2-alkyl-4-isothiazoline 3-one and 5-chloro-2-alkyl-4-isothiazoline-3-one. Numerous methods have focused on purifying 2-alkyl-4-isothiazoline 3-one from the mixture of the composition contaminated with 5-chloro-2-alkyl-4-isothiazoline-3-one (Specification, pp. 1-2). However, none has been successful in purifying 2-alkyl-4-isothiazoline 3-one with sufficiently low amount of 5-chloro-2-alkyl-4-isothiazoline-3-one and minimizing the loss of 2-alkyl-4-isothiazoline 3-one associated with the purification.

Applicants' claimed invention is an industrial disinfectant composition comprising, as an effective component, 2-alkyl-4-isothiazoline-3-one, in which the amount of the contaminant, a 5-chloro-2-alkyl-4-isothiazoline-3-one is less than 0.1%. Applicants achieve this purity level by producing high-purity 2-alkyl-4-isothiazoline-3-one, instead of refining the mixture of 2-alkyl-4-isothiazoline 3-one with 5-chloro-2-alkyl-4-isothiazoline-3-one in the conventional method. In doing so, Applicants discovered that the selectivity of 2-alkyl-4-isothiazoline-3-one varies greatly with the type of solvent used in the reaction and a

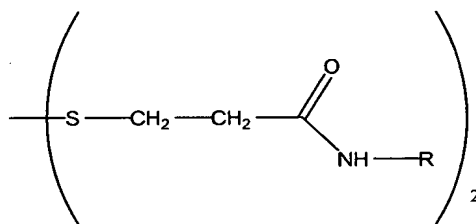
correlation exists between the solubility of the hydrogen chloride in the solvent and the ratio of 2-alkyl-4-isothiazoline-3-one to 5-chloro-2-alkyl-4-isothiazoline-3-one (Specification, p.3, ll. 17-29).

Particularly, Applicants use dichloromethane as a solvent, in which hydrogen chloride is insoluble or exhibit low solubility, and a ratio of two equivalents of chlorinating agent per mole of formula (I), or three mole equivalents of chlorinating agent per mol of formula (II).

Formula (I)



Formula (II)



None of the cited references teach or suggest the use of dichloromethane as a solvent and a ratio of chlorinating agent with reactants.

Lewis et al. (U.S. Pat. 3,849,430) discloses a process for the preparation of substituted 3-isothiazolones and 3-hydroxyisothiazoles by reacting a disulfide-amide or a mercapto-amide with a halogenating agent. Isothiazoles and isothiazolones are prepared by the oxidation cyclization of a di-sulfideamide or a mercapto-amide by contacting the amide with a halogenating agent (Lewis et al. '430 patent, col. 2, ll. 26-46). The '430 patent does not teach or suggest the dichloromethane as a solvent, nor the purity of the 3-isothiazones and 3-hydroxyisothiazoles .

Bayer et al. (U.S. Pat. 5,420,290) discloses a process for preparing 3-isothiazolone substantially free of a by-product, nitrosamine impurities using the amidation of the disulfide intermediates. Bayer et al. also discloses that the biocides contains a 3-isothiazolone mixture comprising mainly 5-chloro-2-methyl-4-isothiazolin-3-one and 2-methyl-4-isothiazolin-3-one (Bayer et al. '290 patent, col. 5, ll. 22-32). Contrary to Applicants' invention, example 1 (Bayer et al., '290 patent, col. 10, ll. 21-26) shows that the final product contains 5-chloro-2-methyl-4-isothiazolin-3-one, 2-methyl-4-isothiazolin-3-one and nitrosamine.

Hahn et al. (U.S. Pat. 5,453,507) discloses a process for preparing 4-isothiazolin-3-one by reacting 3,3'-dithiodipropionic acid with thionylchloride, reacting with amine compound to prepare 3,3'-dithiodipropionamide derivative and adding sulfonylchloride in organic solvent to cyclize (Hahn et al. '507 patent, col. 3, ll. 6-15). Not only the purity of the final product in Hahn et al. (Hahn et al. states "the yield is more than 90%" in col. 3, line 57) is far inferior to Applicants' invention (less than 0.1% of 5-chloro-2-alkyl-4-isothiazoline-3-one), but also type of solvent of Hahn et al. is different from Applicants' invention (toluene or benzene may be used as reaction solvent at col. 3, line 31).

Yen et al. (U.S. Pat. 5,290,512) discloses a use of a mixture of 5-chloro-2-methyl-4-isothiazoline-3-one and 2-methyl-4-isothiazoline-3-one for the disinfection of contact lenses and the preservation of *contact lens care solutions* (Yen et al. '512 patent, col. 2, ll. 4-28). Yen et al. does not teach or suggest an industrial disinfectant composition comprising, as an effective component, a 2-alkyl-4-isothiazoline-3-one, in which the amount of the contaminant, a 5-chloro-2-alkyl-4-isothiazoline-3-one is less than 0.1%.

Lewis et al. (U.S. Pat. 3,523,121) discloses a novel compounds of 3-isothiazolones comprising of 2-carbamonyl and 2-thiocarbamoyl-3-isothiazolones by reacting a 3-hydroxyisothiazole with an isocyanate or isothiocyanate on a substantially equimolar basis (column 4, lines 35-42). Lewis et al '121 patent does not teach or suggest the purity or solvent of Applicants' claimed invention.

Jordan (DE 3702546) discloses a medical disinfectant composition containing isothiazolin-3-ones with ethylene glycol, lauryl ether sulfate, isopropanol, EDTA, perfume

and water. Jordan does not teach an industrial disinfectant composition comprising, as an effective component, a 2-alkyl-4-isothiazoline-3-one, in which the amount of the contaminant, a 5-chloro-2-alkyl-4-isothiazoline-3-one is less than 0.1%,

None of the references, taken alone or in combination, discloses an industrial disinfectant composition comprising, as an effective component, 2-alkyl-4-isothiazoline-3-one, in which the amount of the contaminant, a 5-chloro-2-alkyl-4-isothiazoline-3-one is less than 0.1%. There are distinct and unexpected benefits achieved by limiting the formation of the detrimental contaminant, 5-chloro-2-alkyl-4-isothiazoline-3-one, to a level less than 0.1%. In particular, in view of mutagenicity, the level of 5-chloro-2-alkyl-4-isothiazoline-3-one's should be such that there is no mutagenic effect on the body, and it is also preferred that the level of 5-chloro-2-alkyl-4-isothiazoline-3-one's be as low as possible even within the range of no mutagenic effect. Thus, achieving a level of 5-chloro-2-alkyl-4-isothiazoline-3-one's of less than 0.1% is completely sufficient and far superior to the levels achieved by the prior art.

Furthermore, none of the cited references, taken alone or in combination, teach or suggest preparing such as mixture using chlorine as a chlorinating agent in dichloromethane, in which hydrogen chloride is insoluble or exhibits low solubility, as a solvent at the reaction temperature in the range of 39-41°C, and the ratio of a chlorinating agent per mole to the reactants in order to achieve the unexpected selectivity of 2-alkyl-4-isothiazoline-3-one over a 5-chloro-2-alkyl-4-isothiazoline-3-one as recited the specification and claims in the invention.


In addition, even if the teachings of the references are combined, the processes described therein would still yield a product containing far more than 0.1% of the detrimental contaminant, 5-chloro-2-alkyl-4-isothiazoline-3-one.

For the reasons discussed above, claims 1-6 are patentable under 35 U.S.C. § 103(a) over Lewis et al. (U.S. Patent 3,849,430 – Lewis I), Bayer et al. (U.S. Patent 5,420,290), Hahn et al. (U.S. Patent 5,453,507), Yen et al. (U.S. Patent 5,290,512), Jordan (DE 3702546), or Lewis et al. (U.S. Patent 3,523,121 – Lewis II), each taken alone and in combination with

each other when similar utilities are asserted. Accordingly, Applicants respectfully request that these rejections be withdrawn.

While this application is now believed to be in condition for allowance, should the Examiner find some issue to remain unresolved, or should any new issues arise which could be eliminated through discussions with Applicants' representative, then the Examiner is invited to contact the undersigned by telephone in order that the further prosecution of this application can thereby be expedited.

Respectfully submitted,



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